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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,987	04/06/2007	Khalil Arar	120361	9438

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
09/19/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspt@polsinelli.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,987	ARAR, KHALIL	
	Examiner	Art Unit	
	JOYCE TUNG	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *11-47* is/are pending in the application.

5a) Of the above claim(s) *12,16,20-21,25,28,32,34* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *11,13-15,17-19,22-24,26,27,29-31,33 and 35-47* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/24/2011 has been entered.

The response filed 1/24/2011 to the Office action has been entered. Claims 11-47 are pending. Claims 11, 13-15, 17-19, 22-24, 26-27, 29-31, 33, and 35-47 are examined.

2. Applicant's arguments, filed 1/24/2011, with respect to the rejection(s) of claim(s) 11-38 under 35 U.S.C. 103 over Reed et al. in view of Nikiforov et al. have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as follows

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 11, 13, 15, 19, and 39-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Wengel et al. (20030224377, issued Dec 4, 2003).

Wengel et al. disclose locked nucleic acid (LNA) which can alter nucleic acid hybridization (see pg. 1, [0010]). LNA can be incorporated into nucleic acid strands which provide nucleic acid probes for universal hybridization (see pg. 2, [0019]). LNA can hybridize to other oligonucleotides (the oligonucleotide is interpreted as analytes) (see pg. 2, [0020]). LNA compositions can be used in a wide variety of applications such as PCR primers (see the Abstract), or probes (see pg. 4, [0040]) detecting a target nucleic acid (see pg. 4, [0040]). The probes are incubated with a target molecule under conditions that allow the nucleic acid to hybridize to the target (see pg. 5, [0051] and claim 38). Desirably, the oligonucleotide has a fluorophore positioned in such a way that the hybridized state of the oligonucleotide can be distinguished from the unbound state by a change in fluorescent signal from the nucleotide, for example, a Taqman probe or a Molecular beacon (see pg. 21, [0194] and claim 35). Typical oligonucleotides that contain one or more LNA units with a modified base suitably contain from 3 or 4 to about 200 nucleic acid repeat units, with at least one unit being an LNA unit with a modified base, more typically from about 3 or 4 to about 5, 6, 7, 8, 9, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140 or 150 nucleic acid units, with 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 LNA units with a modified base being present (see pg. 3, [0026]). This inherently teaches that the ratio of LNA moieties to standard nucleic acid moieties in a nucleic acid probe is from about 1:5 to 1:1.4. Thus, the teachings of Wengel et al. anticipate the limitations of the claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 14, 17-18, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wengel et al. (20030224377, issued Dec 4, 2003) as applied to claims 11, 13, 15, 19, and 39-40 in view of Ugozzoli et al. (Analytical Biochemistry, 2004, Vol. 324, pg. 143-152).

The teachings of Wengel et al. are set forth in section 4 above, Wengel et al. do not disclose the limitations of claims 14, 17-18 and 22.

Ugozzoli et al. disclose using oligonucleotide probes containing LNA residues in real-time polymerase chain reaction using the 5'-nuclease detection assay for the detection of single nucleotide polymorphisms (SNPs) (see pg.143, the Abstract). The PCR is multiplex PCR (see pg. 145, column 2, second paragraph).

One of ordinary skill in the art would have been motivated to apply oligonucleotide probes containing locked nucleic acids (LNA) in real time PCR for detecting single nucleotide polymorphisms (SNPs) because Ugozzoli et al. disclose that LNA is incorporated into an oligonucleotide sequence, and the melting temperature of the oligonucleotide is increased considerably, thus allowing the successful use of shorter LNA probes as allele-specific tools in the assay (see pg. 143, the Abstract). It would have been prima facie to use a nucleic acid probe comprising LNA moieties in a real time detection reaction.

7. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wengel et al. (20030224377, issued Dec 4, 2003) as applied to claims 11, 13, 15, 19, and 39-40 above, and further in view of Nikiforov et al. (677184, issued Aug. 17, 2004).

The teachings of Wengel et al. are set forth in section 4 above, Wengel et al. do not disclose the limitations of claims 23.

Nikiforov et al. teach nucleic acid probes derivatized with fluorescent dyes which also comprise monomeric LNA moieties, and the LNA moiety is complementary to the opposing SNP site subsequent to the hybridization of the probes with the target analyte (see col. 7 lines 40-41, where a probe is disclosed which contains a rhodamine label and a LNA moiety, and col. 13, lines 50-67, where SNP detection is disclosed).

One of ordinary skill in the art would have been motivated to use probes containing LNA moieties and a derivatized fluorescent label for use in the detection of SNPs as claimed because Nikiforov et al. teaches that LNAs obey Watson-Crick base pairing rules and hybridize to complementary DNA, RNA or PNA and that LNAs can bind to DNAs or other nucleic acids with higher avidity, affinity and/or specificity than corresponding standard DNAs (see col. 7

lines 14-15 and col. 7 lines 4-6). It would have been prima facie obvious to use probes comprising LNA moieties for detecting SNPs, and that such probes will reduce the incidence of false positives, negatives, and artifacts in the data.

8. Claims 24, 26, 29-31, 33, 35-38 and 42-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (20020197630, issued Dec. 26, 2002) in view of Wengel et al. (20030224377, issued Dec 4, 2003).

Knapp et al. disclose methods for high-throughput genetic analysis such as identifying single nucleotide polymorphisms in patients (see pg. 1, [0009]). The methods use a first probe and a second probe. The first probe and the second probe hybridize to a target nucleic acid comprising a polymorphic variant sequence substantially adjacent to each other (see pg. 3, [0017]). The probes can comprise artificial nucleic acid; for example, LNAs or PNAs (see pg. 2, [0013]). In several embodiments, the probes are labeled with a fluorescence resonance energy transfer (FRET) pair. The changes in the fluorescence of the pair of nucleic acid probes are based upon the hybridization of the pair of nucleic acid probes (see pg. 2, [0015]).

Knapp et al. do not disclose the ratio of LNA moieties to standard nucleic acid moieties in a LNA containing probe as recited in claims 24 and 42-47.

The teachings of Wengel et al. are set forth in section 4 above.

Wengel et al. discusses the ratio of LNA moieties to standard nucleic acid moieties (see pg. 3, [0026]) in desirable oligonucleotides (see pg. [0027] to [0030]). This inherently teaches that the ratio of LNA moieties to standard nucleic acid moieties in a nucleic acid probe is from about 1:5 to 1:1.4.

One of ordinary skill in the art would have been motivated to apply the teachings of Wengel et al. to design probes comprising LNA moieties with a reasonable expectation of success because Wengel et al. disclosed that the probes are used in a wide range of application; for example, PCR (see pg. 4, [0035]), and variation detection (see pg. 4, [0036] & [0039]). It would have been prima facie obvious to use the ratio of LNA moieties to standard nucleic acid moieties in LNA containing probes as claimed.

9. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (20020197630, issued Dec. 26, 2002) in view of Wengel et al. (20030224377, issued Dec 4, 2003) as applied to claims 24, 26-27, 29-31, 33, 35, 37-38 and 42-47 above, and further in view of Heller et al. (5532129, issued Jul. 2, 1996).

Knapp et al. and Wengel et al. do not explicitly disclose that donor and the accepter dyes are within 25 nucleotides of one another.

Heller et al. disclose that the spacing between a donor and acceptor in double stranded DNA polymers is roughly 3 to 7 bases for optimum transfer distance and preferably is about 4 to 6 bases (see column 10, lines 11-14).

One of ordinary skill in the art would have been motivated to apply the spacing between donor and acceptor dyes of a pair of nucleic acid probes within 25 nucleotides of one another because Heller et al. discussed the optimum transfer distance between donor and acceptor. It would have been prima facie obvious to apply the spacing between donor and acceptor dyes of a pair of nucleic acid probes within 25 nucleotides of one another as claimed.

10. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (20020197630, issued Dec. 26, 2002) in view of Wengel et al. (20030224377, issued Dec 4,

2003) as applied to claims 24, 26-27, 29-31, 33, 35, 37-38 and 42-47 above, and further in view of Sanger et al. (Biochemica, 1999, No.2, pg. 7-11).

The teachings of Knapp et al. and Wengel et al. are set forth in section 8 above.

Knapp et al. and Wengel et al. do not disclose the limitation of claim 29.

Sanger et al. disclose the LightCycler System for fast PCR amplification including real-time PCR (see pg. 7, the Introduction). Two different fluorescent molecules hybridize to a target DNA molecule. LC-red 640 and LC-red 705 are used as fluorescence labels. (see pg. 7, column 2).

One of ordinary skill in the art would have been motivated to use LC-red 640 or LC-red 705 in the method as claimed because these dyes have been used in fast PCR amplification as disclosed by Sagner et al. It would have been prima facie obvious to use these dyes in the method as claimed.

12. Jakobsen et al. (EP 1 247 815) is made of record as a reference of interest because it discloses the ratio of LNA moieties to standard nucleic acid moieties in oligonucleotides (see claims 12-20).

Summary

13. No claims are free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JOYCE TUNG whose telephone number is (571)272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joyce Tung/
Examiner, Art Unit 1637
September 10, 2011

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637